REMARKS

Claims 1, 4-6, 9-11, 14-16, 19-21, 24-26, 29-31, 34-44, 47-49, 52-54, 57-59 and 62-66 are pending in this case. With this amendment, claims 31 and 34-39 are canceled, and claims 1, 4-5, 9-10, 14-15, 19-20, 24-26, 29-30, 44, 47-48, 52-53, 57-58, and 62-66 are currently amended without prejudice or disclaimer. Support for the amendments to claims 1 and 44 is found on page 43, line 5 of the application as filed. Support for the amendments to claims 64-66 is found on page 27, lines 29-30. Amendments to claims 4-5, 9-10, 14-15, 19-20, 24-26, 29-30, 47-48, 52-53, 57-58 and 62-63 were made for clarity. The amendments do not add new matter. With this amendment, claims 1, 4-6, 9-11, 14-16, 19-21, 24-26, 29-30, 40-44, 47-49, 52-54, 57-59 and 62-66 are currently pending. Applicants reserve the right to prosecute any canceled or otherwise unclaimed subject matter of this patent application in continuation or divisional applications. Based on the claims and remarks presented below, Applicants submit that the application is now in condition for allowance.

The Examiner's Action

The latest Office Action, dated February 8, 2008, sets forth the following:

-rejection of claims 34 and 35 under 35 U.S.C. 112, second paragraph, as being indefinite; and

-rejection of claims 1, 4-6, 9-11, 14-16, 19-21, 24-26, 29-31, 34, 35, 37, 40-44, 47-49, 52-54, 57-59 and 62-66 under 35 U.S.C. 112, first paragraph for failing to comply with the enablement requirement.

Rejections Under 35 U.S.C. 112, Second Paragraph

Claims 34 and 35 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite. With this response, claims 34 and 35 have been canceled, rendering this rejection moot.

Rejections Under 35 U.S.C. 112, First Paragraph

Claims 1, 4-6, 9-11, 14-16, 19-21, 24-26, 29-31, 34, 35, 37, 40-44, 47-49, 52-54, 57-59 and 62-66 stand rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement. Claims 31, 34, 35 and 37 have been canceled; the rejection as to these claims is therefore moot. Applicants respectfully traverse these rejections as to the other claims as indicated below.

The Examiner alleges that the claims contain subject matter that was not described in the specification in such a way as to enable one of skill in the art to make and/or use the claimed invention. The Examiner states that the specification is not enabling: i) for administering the expression vectors to treat cancer by inducing a therapeutic immune response (page 3 of February 8, 2008 Office Action), ii) for overcoming problems with in vivo delivery and expression of the expression vectors (beginning on page 4 of Office Action), and iii) because tumor cells can escape the immune response by a variety of mechanisms (beginning on page 6 of the Office Action). For example, the Examiner alleges:

> The specification is not enabling for administering the expression vectors to treat cancer by inducing a therapeutic immune response . . . nor is it enabling for a method of treating cancer comprising the administration of peptides derived from BFA4. Claims drawn to an expression vector which further incorporates tumor antigens, angiogenesis antigens or co-stimulatory molecules are included with the rejection as well as pharmaceutical composition because said products are clearly intended to be used for generating a therapeutic response to a BFA4 expressing cancer and the specification does not teach how to use such an expression vector, encoding molecules important for the immune response. (Office Action, pp. 3-4)
>
> The instant specification does not teach how to overcome problems with in vivo delivery and expression . . . in vivo gene delivery is not well developed and highly unpredictable . . . there is no nexus between the transfection of cell in vitro with constructs encoding BFA4, and the successful modulation of the immune response against the BFA4 antigen sufficient to cause a therapeutic effect. (Office Action, p. 4)
>
> Given the lack of any guidance from the specification on any of the above evidence of unreliability on the art, one of skill in the art would be subject to undue experimentation without reasonable expectation of success in order to practice the claimed methods. (Office Action, p. 6)
>
> Thus, it can be concluded that the instant invention would require undue experimentation because as of 2006, four years after the earliest effective filing date claimed,, the art is still immature for how to elicit a clinical benefit from transient gene delivery and predicts that clinical efficacy can be attained within another decade. (Office Action, p. 13)

The Examiner's allegations appear to be directed to the "method of treatment" claims (e.g., use of phrases like "method of treating cancer", "therapeutic effect", "clinical benefit").

Applicants do not agree that claims relating specifically to such methods are not enabled but, to hasten prosecution, have canceled the pending method claims (claims 31, 34-35, 37). All of the remaining pending claims merely recite poxvirus expression vectors for expressing a BFA4 protein in a cell that induces a T-cell response against the BFA4 protein. Claim 1 has been amended to remove recitation of immunogenic fragments and peptides.

As shown below, the specification clearly enables one of skill in the art to construct the instantly claimed poxviral vector and determine whether or not that vector induces a T-cell immune response in a mammal. Therefore, the specification does demonstrate how to make and use the invention as now claimed.

Example 1 of the application describes cloning of a BFA4-encoding nucleic acid, construction of expression vectors containing that nucleic acid, expression of BFA4 from such expression vectors, generation of human T-cells reactive against BFA4 using peptides, and induction of a T-cell response following in vivo administration of such vectors to mice. Synthesis of multiple types of expression vectors encoding the nucleotide sequence for BFA4 and expression of the BFA4 protein from such vectors in cultured cells is described on page 32, line 14 to page 36, line 20 (paragraphs [0084]-[0106] of U.S. 2004/0197912 A1, published October 7, 2004) of the application. Generation of human T-cells reactive against BFA4 is described on page 41, lines 2-19 (paragraphs [0111]-[0113] of U.S. 2004/0197912 A1) of the application. Those studies show that a substantial number of peptides derived from BFA4 did activate human T-cells, as measured by ELISPOT assays and antigen-specific cytotoxic T-cell killing of target cells expressing BFA4 (also see Table VII of the application).

Additionally, the in vivo studies described on page 42, line 25 to page 43, line 5 (paragraphs [0114]-[0116] of U.S. 2004/0197912 A1) significantly extend the in vitro studies discussed above. At least three different types of BFA4-expressing vectors were administered to transgenic mice expressing human HLA-A2 molecules, and all of these were shown to induce a specific T-cell response against BFA4. The transgenic mice utilized in these experiments expressed the human HLA-A*0201 peptide-binding domain such that "human" HLA-A2 restricted, BFA4-specific T-cell immune responses were detected and measured. Such transgenic animals are routinely utilized in such studies and are considered by those of skill in the art to be reasonably predictive of human immune responses. These data show that spleen cells from the immunized transgenic mice, after boosting with BFA4 peptides, secreted IFN-γ as measured in ELISPOT assays. This is indicative of an induced T-cell response against BFA4 protein in the mice expressing human HLA-A2.

Thus, the Examples show and describe how to make and use the claimed BFA4-expressing poxvirus vectors that induce T-cell immune responses against BFA4, as instantly claimed. One of skill in the art is provided with ample guidance as to how to make and use the claimed poxviral vectors as well as how to detect whether or not such vectors induce a T-cell response against BFA4 both in vitro and in vivo. Applicants maintain, therefore, that the specification enables the instantly pending claims. It is therefore respectfully requested that these rejections be withdrawn.

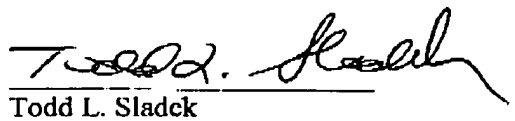
The Examiner also rejected (beginning on page 11 of the February 8 Office Action) claims 4, 5, 9, 10, 14, 15, 19, 20, 24, 25, 29, 30, 34, 35, 47, 48, 52, 53, 57, 58, 62 and 63, alleging lack of enablement for the NYVAC, ALVAC, ALVAC(2) and TROVAC expression vectors. Claims 34 and 35 have been canceled, rendering the rejection as to those claims moot. As to the other claims, Applicants have included with this response copies of deposit receipts/viability statements from the ATCC evidencing deposit of materials related to these viruses under the Budapest Treaty (pages 23-24 of the application as filed). Deposits designated by accession numbers VR-2559, VR-2558, VR-2557, VR-2556, 97913, 97912 and 97914, related to NYVAC, were deposited on March 6, 1997. The deposit designated by accession number VR-2547, related to ALVAC, was deposited on November 14, 1996. The deposit designated by accession number VR-2553, related to TROVAC, was deposited on February 6, 1997. The undersigned Applicants' representative states that these deposits have been accepted by an International Depository authority (ATCC) under the provisions of the Budapest Treaty, that restrictions to public access to the deposits will be removed upon grant of the current application as a patent, and that the deposits will be replaced if viable samples cannot be dispensed from the depository. Additionally, amendments have been made to the specification to recite the date of each deposit as well as the name and address of the depository. Please inform Applicants if anything additional is required as related to these deposits. It is requested that these rejections be withdrawn.

CONCLUSIONS

Consideration and entry of this response is respectfully requested. Applicants believe the claims are now in condition for allowance, and respectfully request that a Notice of Allowance be issued as soon as possible. The Examiner is encouraged to contact the undersigned if it is believed doing so would assist in the examination of this application

Respectfully submitted,

Dated: August 8, 2008

By: 

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